clorazepate (20mg 2×/d), and pregabalin (100 mg 3×/d). Because of resurgence of severe anxio-depressive symptoms, without any change of the treatment, the patient was readmitted 2 months later. Despite increasing the dose of clomipramine up to 225 mg/d, there was no clinical improvement, **and the patient finally attempted to her life by abusing** drugs. She then improved after 2 weeks on clomipramine IV (50 mg/d). Compliance was estimated good and no pharmacokinetic interactions with the rest of the treatment were found. C and DC plasma levels were measured, and CYP2D6/CYP2C19 genotype analyzed.

Results: The plasma levels of C and DC are given in the **Table** below. Measures were done at the steady state and at trough concentration for IV treatment and 10 hours after the last dose for oral treatment.

Table. Doses and plasma levels.

Posology (mg/d)			
Route of administration	150	50	
	oral	intravenous	
C (micromol/l)	0.3-0.8	0.17	0.28
DC (micromol/l)		0.14	0.27
C + DC (micromol/l)	0.8-1.6	0.31	0.55

Clomipramine bioavailability, 50%.

The CYP2D6 genotyping was CYP2D6 *1/*2xN, compatible with an ultrarapid metabolizer. The CYP2C19 genotyping was CYP2C19*1/*1, compatible with an extensive metabolizer.

Conclusion: The lack of clinical effect of oral clomipramine after a dramatic response to IV administration and the low per os plasma levels of clomipramine and its active metabolite, desmethylclomipramine, suggested a rapid phenotype for CYP2D6. This was confirmed by genotyping. This case stresses the value of genotype determination to assess treatment failures in a population of patient wherein lack of compliance is often mentioned.

Disclosure of Interest: None declared.

PP270—COMPUTATIONAL MODELING OF DRAVET SYNDROME

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Introduction: Dravet syndrome (DS) is a rare pediatric epilepsy of early life onset characterized by pharmacoresistant hemi- or generalized (tonic)-clonic seizures and severe cognitive prognosis. The voltage-gated sodium channel SCN1A gene is mutated in 85% of the patients. Transgenic mice models of DS suggest that the mutation specifically involves GABAergic interneurons and leads to selective loss of sodium current affecting their firing properties. However, the mechanisms leading from interictal activity to seizure generation and the subtype of interneurons involved are not known. Computational modeling of neuronal network is currently used to analyze these mechanisms. The inconsistency of firing rate in GABAergic interneurons can be used as a starting point to build a computational model of DS.

Objectives: To find parameters and connections in the model that reproduce EEG patterns of DS patients.

Patients (or Materials) and Methods: We first made a quantitative and qualitative analysis of EEG recorded in DS patients during interictal, preictal, and ictal periods. We next used a lumped-parameter approach (mean-field model) lying at the level of neuronal population and able to represent the generation of spontaneous EEG. This computational model includes 1 subpopulation of pyramidal cells and 2 subpopulations of interneurons (mediating fast and slow GABAergic currents).

Results: EEG signals were characterized by slow background activity (1–4 Hz), multifocal interictal epileptic spikes and, as far as hemi-clonic seizures were concerned, by fast oscillations at the onset of seizures. To mimic the effect of a SCN1A mutation, the firing rate of GABAergic current was modified in slow interneurons. Preliminary results show that appropriate alterations in the strengths of GABAergic and glutamatergic connections, and in the amplitudes of average EPSPs/IPSPs in the model successfully lead to slow background activity (1–4 Hz), generation of interictal epileptic spikes, and fast onset activity and seizure-like activity.

Conclusion: Our computational modeling of DS is therefore promising. Further optimization is needed for reproducing all the features of the real EEG from patients and identifying the key parameters of specific EEG patterns.

Disclosure of Interest: None declared.

PP271—NOVEL THERAPEUTIC STRATEGY TO PREVENT CHEMOTHERAPY-INDUCED PERSISTENT SENSORY NEUROPATHY BY TRPA1 BLOCKADE

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Introduction: Several anticancer medicines evoke sensory adverse events, collectively referred to as chemotherapy-induced peripheral neuropathy (CIPN), which are represented by sensory symptoms. No effective therapy is currently available to treat or prevent CIPN, most likely because the underlying mechanisms are poorly understood. A host of hypotheses has been proposed to explain CIPN, but nonetheless no unified mechanism that may reconcile results of clinical investigation and findings obtained in experimental animals has been advanced so far. Chemotherapeutic drugs, which produce CIPN, are known to increase oxidative stress and reactive oxygen, nitrogen, or carbonyl species (ROS, RNS, and RCS, respectively) and treatment with antioxidant substances has been shown to reduce sensory hypersensitivity in experimental animals and to exhibit some degree of protection in patients with CIPN. The transient potential receptor ankyrin 1 (TRPA1) is a nonselective cation channel, coexpressed with TRP vanilloid 1 (TRPV1) in a subset of C-fiber nociceptors, where it functions as a multimodal sensor to noxious stimuli. TRPA1 shows a unique sensitivity for an unprecedented number of endogenous reactive molecules produced at sites of tissue injury or inflammation, which include ROS, RNS and RCS. Bortezomib is a proteasome inhibitor used indifferent types of cancer. CIPN has